REMARKS

Claims 8-28 are active in this application.

Applicants wish to thank Examiner Rao and Examiner Prouty for the helpful and courteous discussion granted to the Applicants' undersigned representative on August 27, 2003. During this meeting, various amendments were discussed to address the rejections of 35 U.S.C. § 112, first and second paragraphs. These amendments and this discussion are reflected in the amendments and remarks submitted herein.

At the outset, Applicants wish to thank the Examiner for the indication that Claims 8-12 are allowable (paper number 11, page 9). Applicants also wish to thank the Examiner for the helpful suggestion to overcome the rejection under 35 U.S.C. §112, second paragraph.

The rejection of Claims 13-20 under 35 U.S.C. §112, first paragraph (enablement), is respectfully traversed.

Applicants note that it appears that the Examiner has based this ground of rejection on the difficulties associated with identifying polynucleotides that when transferred into a bacterium increases the homoserine resistance of the bacterium and are 70% homologous to or hybridizes to the sequence of SEQ ID NO:1 or nucleotides 557 to 1171 of SEQ ID NO:1. Applicants submit that the present invention does adequately enable the skilled artisan to make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. Specifically, Applicants submit that with the present specification in hand it would be well within the purview of the skilled artisan to determine which

polynucleotides when transferred into a bacterium increases the homoserine resistance of the bacterium and are 70% homologous to or hybridizes to the sequence of SEQ ID NO:1 or nucleotides 557 to 1171 of SEQ ID NO:1.

MPEP § 2164.01 states:

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Applicants submit that determining what sequences fall within or without the scope of the present claims would be readily apparent to the skilled artisan with the present application in hand. Applicants note that provided with the nucleotide sequence in SEQ ID NO: 1 and the tools necessary to hybridize one DNA to another DNA and determine whether it has the necessary homology and activity is within the well-described knowledge available in the art. In support of this knowledge, Applicants submitted a selected portion from "Short Protocols in Molecular Biology" unit 2.10, which describes hybridization analysis of DNA (third edition, Compendium of Methods From Current Protocols and Molecular Biology, Ausubel et al (eds.) John Wiley and Sons, Inc., New York) and a homology search with the rhtB sequence from *E. coli* using the BLAST and FASTA search engines, with their response of April 2, 2003, as illustrative of the ability to ascertain the percent homology between two nucleotide sequences.

Despite the knowledge available in the art, the Examiner states: "producing and using polynucleotides as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property" (page 7 of paper number 11). The guidance that the Examiner purports as lacking include: (A) regions of the DNA sequence which may be modified without effecting the activity/utility; (B) the general tolerance of homoserine resistance imparting

DNA sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide sequence with an expectation of obtaining the desired biological function and utility; (D) specific high-stringency hybridization conditions; and (E) guidance as to which mutant would be successful.

Regarding these points raised by the Examiner, Applicants wish to note that RhtB is a transmembrane protein that is highly hydrophobic and contains 5 possible transmembrane segments (see page 21, lines 21-23). The lysE gene is similar to the rhtB gene in encoding for a protein related to amino acid efflux and has highly conserved transmembrane segments (see Vrljic et al, J. Mol. Microbiol. Biotechnol., 1999 Nov; 1(2): 327-336, **copy enclosed**). Based on the similarity of function between the rhtB gene and the lysE gene, it would be apparent to the artisan that the transmembrane segments of the rhtB gene product are also highly conserved. Therefore, by performing PCR using primers designed based on the sequences of the transmembrane segments of RhtB, the skilled artisan can easily obtain DNA fragments encoding transmembrane segments of RhtB variants. Clearly such PCR methods would not require undue experimentation as this technique is a hallmark of modern biochemistry and genetic research. Therefore, ascertaining and cloning of genes that are 70% homologous to or hybridizes to the sequence of SEQ ID NO:1 or nucleotides 557 to 1171 of SEQ ID NO:1 would be enabled with the present specification in hand.

MPEP §2164.04 states:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

At page 6, line 15 to page 11, line 10, Applicants provide a detailed explanation of how the skilled artisan may clone, identify, and vary the sequence of the rhtB gene. At page 11, line 11 to page 13, line 12, Applicants provide an explanation of mechanisms by which the Rh activity may be enhanced as well as bacterial transformations to accomplish the same. At page 17, line 14 to page 19, line 9, Applicants highlight the method for producing amino acids and recovering the same. This detailed description in and of itself would be sufficient when coupled to enable the skilled artisan to clone, express, and characterize the polynucleotides that fall within the scope of the present invention, especially when coupled with the knowledge generally available in the art.

Applicants have not stopped here in their description to provide the artisan with sufficient information by which to identify polynucleotides that fall within the scope of the present invention, as Applicants have provided a highly detailed series of Examples (pages 19-28) despite no requirement for providing the same. Applicants remind the Examiner that the MPEP further states in §2164.02:

> The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

Of particular interest, Applicants wish to direct the Examiner's attention to Example 5 (page 26). In Example 5, Applicants provide a detailed summary of how the artisan may determine the activity of a bacterium expressing the polynucleotides falling within the scope of the present invention to assess whether the gene product imparts L-homoserine resistance. Specifically, in Example 5 the activity of strain N99/pRhtB, in which a DNA having a homology of at least 70% to a nucleotide sequence of SEQ ID NO:1 is amplified, is determined by using test plates with M9 agar containing L-homoserine. By using these plates

as described in Example 5, the artisan may easily determine whether or not a DNA fragment has the activity set forth in the claimed invention.

In view of the foregoing, the act of obtaining and screening candidate polynucleotides can be performed routinely. Therefore, identifying DNA sequences that encode a protein having the desired activity and claimed homology would be well within the purview of the skilled artisan without requiring undue experimentation.

Moreover, based on the Examiner's comments on page 7 of paper number 11, it appears that the Examiner is confusing "quantity of experimentation" with "undue experimentation," MPEP §2164.06 states:

> ... quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Applicants submit that, with the present specification in hand, determination of polynucleotide sequences that fall within the scope of the present invention would require nothing more than routine experimentation to determine sequence homology and protein activity. As such, Applicants submit that the claims of the present application are fully enabled within the context of 35 U.S.C. §112, first paragraph.

Based on the foregoing, Applicants submit that the present claims are fully enabled by the specification and the common knowledge available in the art and as such withdrawal of this ground of rejection is requested.

The rejection of Claims 17-20 under 35 U.S.C. §112, first paragraph (written description), is obviated by appropriate amendment.

Claim 17 has been amended to recite: "wherein the mutant DNA is not less than 70% homologous to nucleotides 557 to 1171 of SEQ ID NO:1." Applicants submit that with this amendment Claim 17 is adequately described in the present specification for the reasons previously of record.

Specifically, Applicants note that provided with the nucleotide sequence in SEQ ID NO: 1 and the tools necessary to hybridize one DNA to another DNA and determine whether it has the necessary homology and activity is within the well-described knowledge available in the art. In support of this knowledge, Applicants submitted a selected portion from "Short Protocols in Molecular Biology" unit 2.10, which describes hybridization analysis of DNA (third edition, Compendium of Methods From Current Protocols and Molecular Biology, Ausubel et al (eds.) John Wiley and Sons, Inc., New York) and a homology search with the rhtB sequence from *E. coli* using the BLAST and FASTA search engines, with their response of April 2, 2003, as illustrative of the ability to ascertain the percent homology between two nucleotide sequences.

Applicants again direct the Examiner's attention to the U.S. PTO "Synopsis of Application of Written Description Guidelines" and, in particular, Example 9 for the standard for written description. In this Example a situation that is similar to Claim 17 is presented. The conclusion is that the claim in the Example, which is similar to Claim 17 in terms of providing for a sequence that hybridizes under stringent conditions to an allowable DNA, is adequately described. Thus, Claim 17 (and the claims dependent on Claim 17) is described because "a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and

knowledge in the art are adequate to determine that applicant was in possession of the claimed invention." (Example 9 of the "Synopsis").

In view of the foregoing, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 13-16 under 35 U.S.C. §112, second paragraph, and the objection of Claim 13 are obviated by appropriate amendment. As such, Applicants note that Claims 13-16 are free from the Examiner's criticism and, therefore, this ground of rejection and the objection of Claim 13 should be withdrawn.

Acknowledgement that this ground of rejection and this ground of objection have been withdrawn is requested in the next action on the merits.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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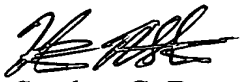

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